



CASE REPORTS

Hyperthyroidism Associated with Presumptive Acute Pericarditis— A Report of Three Cases

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THE ASSOCIATION of hyperthyroidism and acute pericarditis is rarely reported in medical literature. Green and Hurxthal² listed one case of pericarditis in a data chart of associated findings in 469 thyrocardiac patients, but no further information about this case was presented. Levy,⁴ in a review of 27 cases of acute serofibrinous pericarditis of undetermined cause, mentioned no instance of the association of hyperthyroidism with pericarditis. Brown¹ presented an excellent basic review of pericarditis but again there was no mention of any association with thyrotoxicosis. Furthermore, in personal communications from several authorities, a considerable difference of experience regarding the frequency of this association was noted.

Recently we observed three patients with hyperthyroidism associated with acute pericarditis. All three cases occurred in middle aged women. The pericarditis in each instance followed the symptomatic course of acute benign pericarditis of probable viral origin.* There were progressive electrocardiographic changes compatible with the patterns associated with pericarditis. Also in each instance the thyrotoxicosis was rather typical from the standpoint of signs, symptoms and laboratory confirmation.

REPORTS OF CASES

CASE 1. The patient was a 37-year-old white woman, who was first observed the morning after a night during which she became acutely ill with severe retrosternal pain of pressure type and dyspnea. She said that the illness started about an hour after the evening meal and then increased in intensity during the night.

*Although Coxsackie is the only virus so far isolated from some cases of "viral pericarditis," it is assumed that acute infectious pericarditis of the benign variety here referred to is of viral origin.

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The blood pressure was 125/80 mm. of mercury, the pulse rate 116 per minute, and there was a gallop rhythm; and a definite pericardial friction rub over the left parasternal area. The patient was obviously short of breath, in definite discomfort and appeared very restless and apprehensive. An electrocardiogram taken immediately was definitely abnormal, showing inverted T waves in Leads 1 and 2, AVL, and V3 to V6. The ST segments were iso-electric, slurring into the T wave inversions (Figure 1).

Admitted to hospital, the patient was given oxygen by mask and morphine sulfate to relieve the pain and restlessness. Moderate pain in the chest and shortness of breath continued, however. After two days, when the acute symptoms had subsided, the clinical appearance suggested thyrotoxicosis. The skin was warm and moist, there was persistent tachycardia and palpitation, tremor and extreme emotional tension; and the general demeanor was almost hypomaniac. It was elicited that for the preceding two months the patient had had vague palpitations, tachycardia, shortness of breath, weakness and occasional vague pain in the chest. The pains at that time also seemed to occur after meals but were very mild and nothing like the rather severe pain which occurred at the onset of the acute illness. The patient stated that also during this period she had noticed increasing hunger and food intake, increased nervousness and tremors; and she said she had become very "warm-blooded." The patient had always been high-strung and emotional, but also during the period preceding acute illness these tendencies had become more evident.

Other physical signs suggesting exophthalmic goiter were: Tremor, a definite droop of the eyelids, persistence of the rapid pulse and the presence in the neck of a palpable diffuse goiter.

Serial electrocardiograms showed the ST segments of Leads V2 and V6 to become slightly elevated or iso-electric and the T waves to become more deeply negative. Q waves did not develop. X-ray films of the chest showed slight cardiac enlargement without any specific change in cardiac configuration.

Rarely did the body temperature not exceed 99.2° F. The leukocyte content varied from 4,100 to 6,700 cu. mm. and there was no increase in poly-

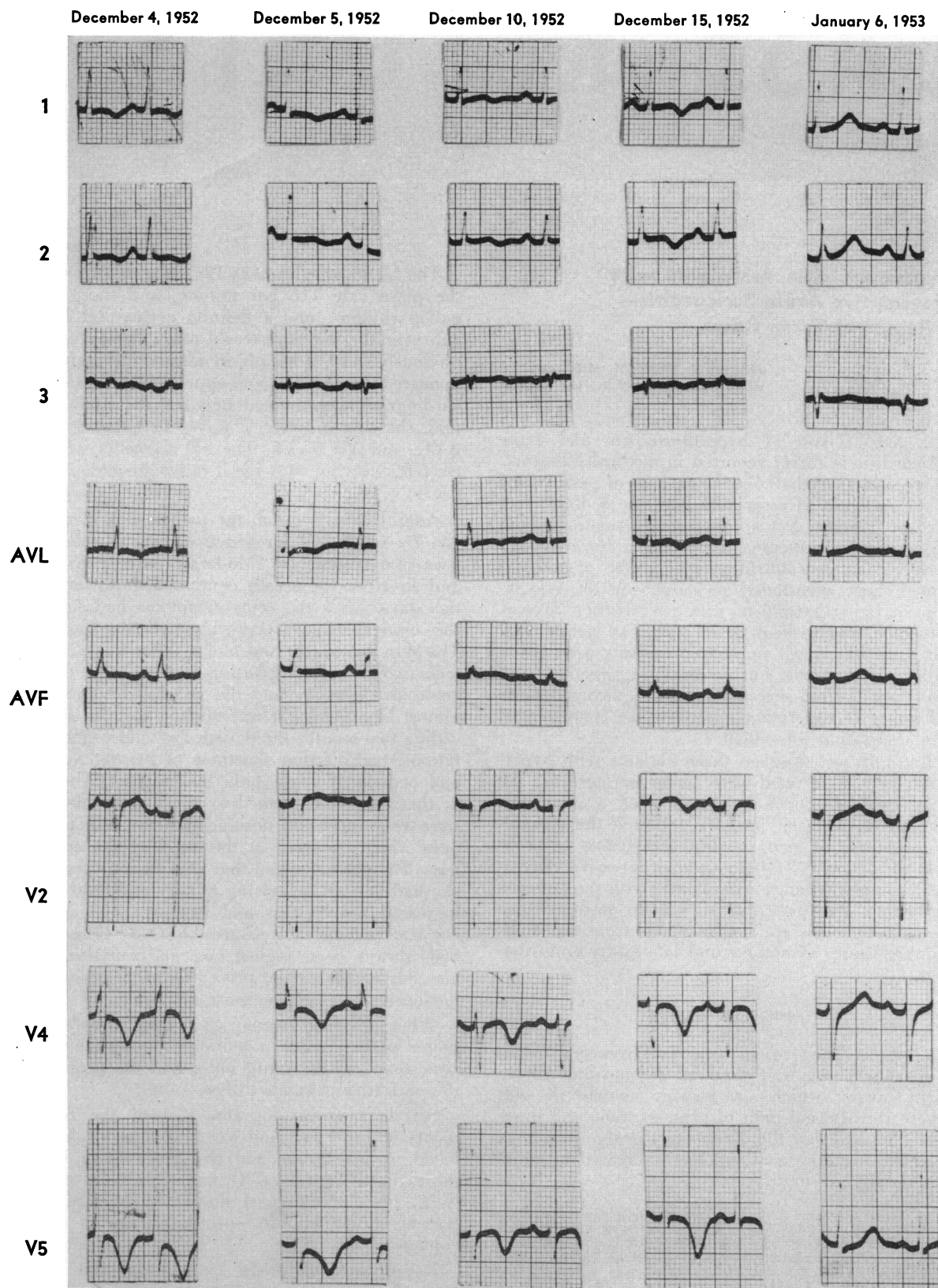


Figure 1.—Electrocardiograms made at various times during illness and after recovery.

morphonuclear leukocytic cells. In fact, at one time lymphocytes made up 62 per cent of leukocytes. The Wintrobe sedimentation rate, 13 mm. in one hour on admission to the hospital, rose to 22 mm. three days later and then slowly decreased (it was determined at three-day intervals) to 12 mm. two weeks later.

These conditions of the blood and the electrocardiographic changes favored the diagnosis of acute pericarditis, rather than acute myocardial infarction, which had to be considered at first. The pericardial friction rub also favored the diagnosis of pericarditis in that it persisted on and off for ten to twelve days. Tachycardia also persisted. Blood plasma iodine content on the seventh hospital day was 10.8 gamma per 100 cc., and when determined again two days later it was 10.3 gamma per 100 cc. Radioactive iodine uptake 24 hours after a test dose of five microcuries was 76.6 per cent. The next day, therefore, an oral therapeutic dose of 5.45 millicuries of radioiodine was given. We felt that it was very important for the treatment of thyrotoxicosis to be started as soon as possible, because the toxic state was probably aggravating the pericarditis, and vice versa. Other therapy included bed rest, sedation, aureomycin, one gram per day in divided doses for six days, and oxygen on and off for shortness of breath and pain in the chest. Except for the several emotional crises, partly related to the stimulation by the thyrotoxicosis and the toxicity of the infection and partly related to the patient's tense and high-strung basic personality, the course was progressively favorable and one of improvement.

On the eleventh day (the fourth day after the therapeutic dose of radioactive iodine¹³¹) the patient seemed particularly jittery and tense. Administration of Lugol's solution, 5 drops three times a day, was begun.

Two months after the first treatment dose of I¹³¹ was given, the radioiodine uptake was 52.8 per cent. An additional 3 millicuries of radioiodine was given orally. Three months later the I¹³¹ uptake was 42.2 per cent, and six months after the first treatment was given it was 35 per cent. At this time the pulse, which during the acute illness ranged from 90 to 104 per minute, was 72 per minute. One year after treatment the patient appeared well and had no complaints and the uptake of iodine was in the upper borderline range, 44.5 per cent. The electrocardiogram had returned to within normal limits.

CASE 2. The patient was a 50-year-old woman who was under treatment for hyperthyroidism. Before treatment with radioactive iodine¹³¹ was started for this patient, the protein-bound iodine content of the blood had been 11.5 gamma per 100 cc. and the radioactive iodine uptake had been 52 per cent. On October 29, 1952, the patient received a dose of radioactive iodine—the only one she received. She had been getting on fairly well and had been back at work for a few days when she first noted slight pain in the chest. That night and the next day she had a severe "crushing" substernal pain, radiating

to the left side and back of the neck. 100 mg. of meperidine intramuscularly was required for relief. The pain persisted despite the administration of Empirin Compound with codeine, 30.0 mg. at intervals, for nine days. During this time the temperature had been slightly elevated each evening, up to 101.8° F., and then gradually subsided.

The patient was put in hospital. The maximum Wintrobe sedimentation rate was 35 mm. in one hour; and the rate then slowly decreased to 10 mm. in one hour in three weeks. The pulse was described as irregular, varying in both rate and rhythm. The patient was treated as having an intercurrent viral infection, and several injections of procaine penicillin were given. The heart rate became regular at 64 beats per minute. At the time of admission to the hospital a friction rub was heard all over the precordium, loudest at the base of the heart. This persisted for several days. The electrocardiogram was described as follows: "T1 negative; ST segment in Leads 2 and 3 slightly depressed with T in Lead 2 flattened; T in Lead AVR diphasic and flattened; T in AVL, negative; marked elevation of ST segment in Leads V1 and V2; T negative in V4 and diphasic in V5 and V6." Subsequent progressive changes in electrocardiograms were those of pericarditis. A week after admittance the electrocardiogram showed: "T waves were inverted in Leads 1, 2, 3 and AVF. The T in AVL was flat. ST segments were elevated in V3 and 4. The T was inverted in V4 and 6. Impression: Abnormal electrocardiogram consistent with pericarditis." One week later a tracing was reported as showing: "Less T wave inversion (almost iso-electric) than previously in Leads 1, 2, 3, AVF and V6. T wave inversion appears in V1 to 3. Impression: Abnormal electrocardiogram consistent with pericarditis."

The report on an electrocardiogram made three weeks after admittance to hospital was: "T waves are flat in Leads 1 and AVL and slightly inverted in Leads 2, 3 and AVF. There is slight terminal inversion of T waves in Leads V3 to 6. As compared with the last previous tracing, there is slight change in the T waves in Leads 1 and AVF, and the T waves of the precordial leads show less inversion. Impression: Abnormal electrocardiogram consistent with pericarditis. Improvement from previous tracing."

There was a Grade 3 systolic murmur, and the above described pericardial friction rub persisted for several days. Two roentgenograms of the chest, one taken ten days after admittance to hospital and the other two days later, showed an area of consolidation in the left upper lobe, probably an area of infarction. In addition, the films showed a slight amount of pleural effusion on the left side as well as a slight pericardial effusion. A film taken a week later showed improvement in the infiltration, but the cardiac shadow still was enlarged.

After radioiodine treatment the patient became relatively hypothyroid and required small doses of desiccated thyroid for maintenance. She no longer had pain, and when observed seven months later

she looked well and said that she felt very well as long as she was taking 30.0 mg. of desiccated thyroid a day. The patient was in a euthyroid state and an electrocardiogram was within normal limits.

CASE 3. A 38-year-old white woman, when first observed, May 11, 1953, had severe precordial pain, radiating backward and into the left arm, of a week's duration. At other times she had had severe pain in the left side of the chest and under the sternum. She also said she had some dyspnea, excessive perspiration, more pronounced at night and palpitation.

When examined, the patient was apprehensive and very nervous, and complained of pain in both shoulders and the left precordium. The blood pressure was 120/80 mm. of mercury. The heart tones were hyperactive and there was definite tachycardia with an apical and radial rate of 116 per minute. There was a slight generalized hyperreflexia. Slight elevation of temperature was noted; usually it was about 99° F., on one occasion 100° F. The Wintrobe sedimentation rate, which was 8 mm. in one hour at the first examination, rose to a maximum of 20 mm. in one hour.

An electrocardiogram taken on May 13 was described as compatible with coronary heart disease or pericarditis, showing inverted T waves in Leads 2, 3 and AVF with slight ST elevation in AVL. At this time, the venous pressure was recorded as 7 mm. of water, the arm to tongue circulation time was 17 seconds, and the arm to lung circulation time was 6 seconds. Protein-bound blood iodine content was reported as 5 gamma per 100 cc.; two weeks later it was still at that level. On May 20 the pain in the precordium began to lessen and electrocardiograms, which were made serially, began to stabilize. The progressive changes in the electrocardiograms showed essentially progressive deepening of the T waves in Leads 2, 3 and AVF, without change in the QRS complexes, indicative of an acute myocardial process. On May 23, the electrocardiogram was within normal limits with upright T's in all leads, except 3, where the T wave had changed from inversion to diphasic. All of these T waves became upright, except the T in Lead 3, where the inversion became less.

On May 29 radioiodine uptake studies were carried out and the thyroid gland uptake was found to be 55 per cent. It has been observed that protein-bound iodine may be normal and the I^{131} uptake may be elevated in a certain number of patients with thyrotoxicosis.³ The patient was given an oral treatment dose of radioiodine (I^{131}) of 2.73 millicuries on May 29, of 2.85 millicuries on June 1, and of 3.9 millicuries on June 9.

Response to radioiodine therapy was good, and by November the patient was able to resume normal activity. When last seen, some 11 months after she was first observed, she was euthyroid and the electrocardiogram was reported to be within normal limits.

DISCUSSION

It is believed that these three cases are worthy of reporting for several reasons. First, the coexistence of a benign (apparently viral) pericarditis and exophthalmic goiter with hyperthyroidism is apparently rare. The infrequency of this association suggests that it is only fortuitous. On the other hand, pericarditis, like any other infection or toxic process, might cause flaring of latent or low grade hyperthyroidism. Furthermore, it is known that resistance to infection in general is usually somewhat lowered in the hyperthyroid state.

Although myocardial complications with friction rubs and dull chest pain occur not infrequently in acute severe hyperthyroidism, well-documented instances of acute pericarditis with the usual course of electrocardiographic findings have not been described. In the three cases reported here, we believe it is fair to say that both conditions (hyperthyroidism and acute pericarditis) were probably associated. A conclusion as to whether this association was fortuitous or there was a more concrete relationship cannot be drawn from the evidence we were able to present.

Because of the paucity of literature on this topic, we decided to write to several authorities for their comments and experience regarding the association of hyperthyroidism and acute pericarditis. We received the following replies:

Arlie Barnes of Rochester, Minnesota, was the only cardiologist who remembered having seen several instances of acute pericarditis combined with hyperthyroidism. His comments were as follows:

"[I saw] great numbers of toxic goiter cases before the advent of iodine in the treatment of exophthalmic goiter. Not uncommonly I saw acute pericarditis in goiter patients, particularly with exophthalmic goiter, and it became so that it was one of the inflammatory complications that we were on particular watch for. We also saw frequent flares of tonsillitis in these patients. We assumed that both of these developments were indicative that their resistance to infection was greatly impaired in the presence of exophthalmic goiter. It was our opinion that the pericarditis encountered in these hyperthyroid patients ran a fairly benign course, although generally they ran the temperature up and were a source of worry and some [were] very sick patients. [Today] hyperthyroidism is nowhere near as toxic as it used to be. Iodine is frequently used early in controlling toxicity and the fact that pericarditis is not a rare complication of hyperthyroidism under present circumstances may make it desirable to make it known that even now the association is not too uncommon."

Paul D. White of Boston said:

"I . . . don't recall any such instance in my own experience. Hence, naturally since I have seen a good many cases of thyrotoxicosis and a good many cases of pericarditis, I would regard it probable that your three cases are coincidental. However, I

cannot be so dogmatic as to say that such a related combination is impossible. Of course it is important to recognize two points, namely, that one may have so much activity of the heart in thyrotoxicosis that there can actually be sounds like a pericardial friction rub chiefly over the conus and pulmonary artery, and, secondly, with tachycardia in thyrotoxicosis the T waves can be depressed without any actual pericarditis."

Robert L. Levy of New York:

"I do not know of any instance of pericarditis associated with hyperthyroidism in which a direct relationship existed between the two conditions. It is difficult to see how thyrotoxicosis would cause a disturbance in the pericardial sac. The association in hypothyroidism, of course, is well known and has been commented upon in the literature."

Samuel Haines of Rochester, Minnesota:

"I haven't seen [the] association recently, but I do remember that many years ago I [saw at least a few such] cases. Whether the association was anything more than coincidental I never knew." "I have the impression that acute pericarditis, along with various other infections, may have been seen more frequently in the past than would have been expected, but this has not been noted by me recently."

Samuel A. Levine of Boston:

"I think that your experiences with acute pericarditis and thyrotoxicosis are rather unique. I recall seeing one such example years ago. It certainly is not a common combination amongst thyrocardiacs, as I have seen a good many masked thyrocardiacs without observing acute pericarditis. Acute rheumatic fever I have seen in patients who also had active hyperthyroidism."

Despite the apparent lack of reported cases and in spite of the limited experience (with one exception) of the consulted authorities with the associa-

tion of hyperthyroidism and acute pericarditis, we believe the combined condition probably does exist more often than this evidence would indicate. It is hoped that our report will stimulate others not consulted to report their experiences. It was certainly true in our cases that the two conditions were mutually aggravating, and it was felt that because of this mutual potentiation of the two processes involved, these cases were ideal for prompt therapy of the hyperthyroidism with radioactive iodine. As a matter of fact, cases of hyperthyroidism with any infectious complication requiring prompt therapy without the risk of operation seem particularly amenable to this form of therapy.

SUMMARY

Three cases of hyperthyroidism associated with pericarditis have been presented.

No case reports of this association could be found in a review of the literature.

The three patients were treated with radioiodine¹³¹ and showed a favorable response.

Personal communications from five authorities from the fields of cardiology and thyroid disease showed (with one exception) infrequent experience with the combination or association of these two disease entities.

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Phlebothrombosis of Subcutaneous Tissue Of Breast (Mondor's Disease)

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MONDOR'S DISEASE was observed by Flagge in 1869 and described as follows: "Anyone familiar with the contents of our museum will remember this model of the breast which presents a deep, puckered groove, looking exactly as if it were a scar after an operation for the removal of the organ and extending into the axilla." Fiesinger and Mathieu in 1922, Faure and Sedallian in 1929 and Huc in 1930 described a disease similar in identity. In 1931 Wil-

liams, and in 1932 Daniels, published reports of several cases resembling this disease. However it was not until 1939 that Henri Mondor, a French surgeon, first described the disease entity which bears his name. He reported cases he had observed and collected reports of several others. Leger, in 1947, collected reports of 22 cases from the literature and discussed the etiology, symptoms, pathologic features and treatment. In a recent review of the American literature I was unable to find any additional information on this syndrome.

The incidence of the disease is highest in women between the ages of 21 and 55 years. The lesion begins as a cord-like band adherent to the skin and subcutaneous tissue with retraction of the skin giving it the appearance of a groove. This cord-like

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